



## **ATTACHMENT B**

### **Amendments to the Claims**

*This listing of claims will replace all prior versions, and listings, of claims in the application.*

1. (Current Amended) An isolated polypeptide comprising an amino acid sequence encoded by the nucleic acid sequence SEQ ID NO: 3, said isolated polypeptide being a membrane-bound metalloprotease referred to as "NEP2" and belonging to the endothelin converting enzyme/neprilysin/Kell family of metalloproteases.

2. (Previously Presented) An isolated nucleic acid comprising the nucleotide sequence SEQ ID NO: 3, or the complementary sequences thereof.

3. (Currently Amended) An oligonucleotide probe consisting of a nucleotide sequence chosen from the group consisting of sequences SEQ ID NO: 5 to SEQ ID NO: 27.

4. (Original) A cloning and/or expression vector containing a nucleotide sequence as claimed in claim 2.

5. (Original) A host cell transfected with a vector as claimed in claim 4.

6. (Previously Presented) Mono- or polyclonal isolated antibodies or their fragments, chimeric isolated antibodies or immunoconjugates, characterized in that they

are obtained using a polypeptide as claimed in claim 1 administered to an animal, and are capable of recognizing specifically a polypeptide as claimed in claim 1.

7. (Withdrawn) A method for immunologically detecting NEP II in a cell or tissue sample or in cells or a tissue, comprising the steps consisting in:

- bringing said cell or tissue sample, said cells or said tissue into contact with a detectable antibody as claimed in claim 6;
- detecting the presence of said antibody, which is an indication of the presence of the NEP II polypeptide.

8. (Withdrawn) A method for detecting the expression of the NEP II polypeptide in a cell or tissue sample or in cells or a tissue, by *in situ* hybridization, comprising the steps consisting in:

- preparing the RNA of said sample or of said cells or of said tissue;
- bringing said RNA obtained into contact with at least one probe having a nucleotide sequence which is capable of hybridizing specifically with a nucleotide sequence as claimed in claim 2, said probe possibly being in particular an oligonucleotide probe as claimed in claim 3;
- detecting the presence of mRNA hybridizing with said probe, which indicates the expression of the NEP II polypeptide.

9. (Withdrawn) A method for detecting the expression of the NEP II polypeptide in a cell or tissue sample or in cells or a tissue, by *in situ* hybridization, comprising the steps consisting in:

- preparing the RNA of said sample or of said cells or of said tissue;
- bringing said RNA obtained into contact with at least one probe having a nucleotide sequence which is capable of hybridizing specifically with a nucleotide sequence as claimed in claim 2; and
- detecting the presence of mRNA hybridizing with said probe, which indicates the expression of the NEP II polypeptide.

10. (Withdrawn) A method for detecting the metalloprotease activity of NEP II in a cell or tissue sample or in cells or a tissue, comprising the steps consisting in:

- bringing said cell or tissue sample, said cells or said tissue into contact with a compound which is a substrate for the NEP II polypeptide, obtained according to the method of claim 9, said substrate compound being optionally labeled;
- evaluating the cleavage of said substrate compound, which is an indication of the metalloprotease activity of NEP II.

11. (Previously Presented) A method for screening compounds which are capable of inhibiting the metalloprotease activity of the NEP2 polypeptide as claimed in claim 1; said method comprising the steps of:

measuring NEP2 activity in the presence or absence of a test compound, under conditions sufficient for NEP2 activity to be measured in the absence of a test compound, and

comparing NEP2 activity as measured in the presence of the test compound with that measured in the absence of the test compound,  
wherein a decreased activity in the presence of the test compound is indicative of a compound capable of inhibiting the metalloprotease activity.

12. (Withdrawn) A method for detecting NEP II in a cell or tissue sample or in cells or a tissue, comprising the steps consisting in:

- bringing said cell or tissue sample, said cells or said tissue into contact with a compound which is a substrate for the NEP II polypeptide, obtained according to the method of claim 9, or with a compound which is a inhibitor of the metalloprotease activity of NEP II, said substrate compound or said inhibitor compound being labeled; and
- detecting the presence of said substrate compound or of said inhibitor compound, which is an indication of the presence of the NEP II polypeptide.

13. (Previously Presented) The method according to claim 11 further comprising manufacturing a medicinal product from the compounds which are capable of inhibiting the metalloprotease activity of the NEP2 polypeptide.

14. (Cancelled)

15. (Cancelled)

16. (Cancelled)